Human-to-cattle transmission of *Mycobacterium tuberculosis* complex species

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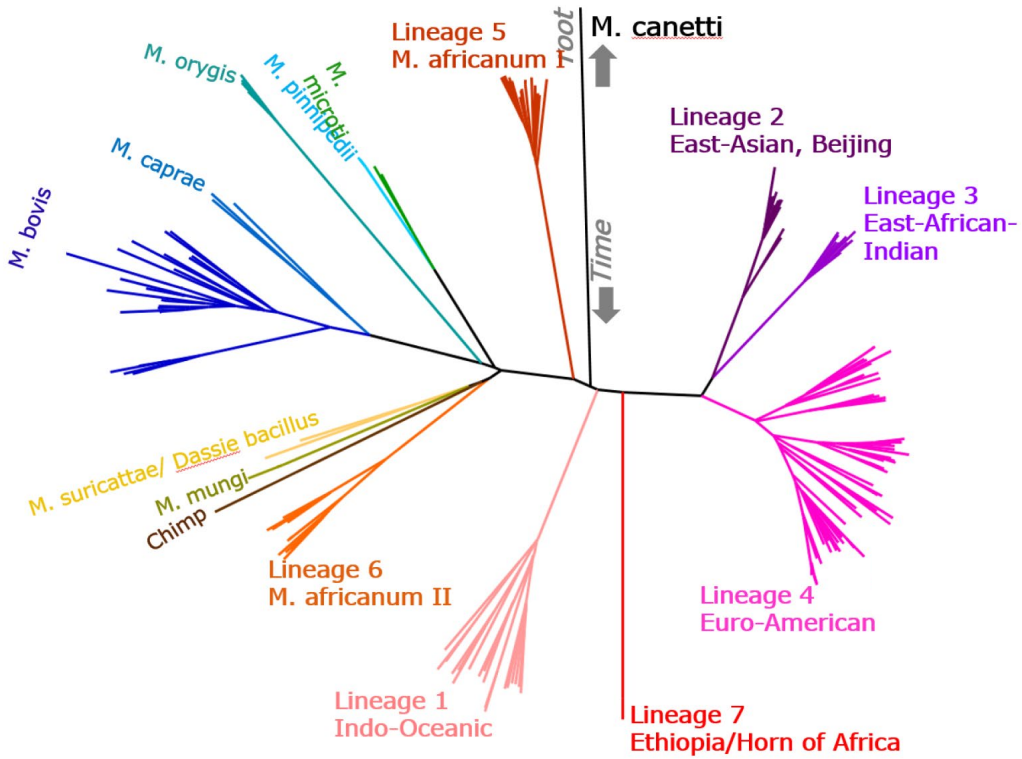
TB Controllers Webinar

November 2, 2021

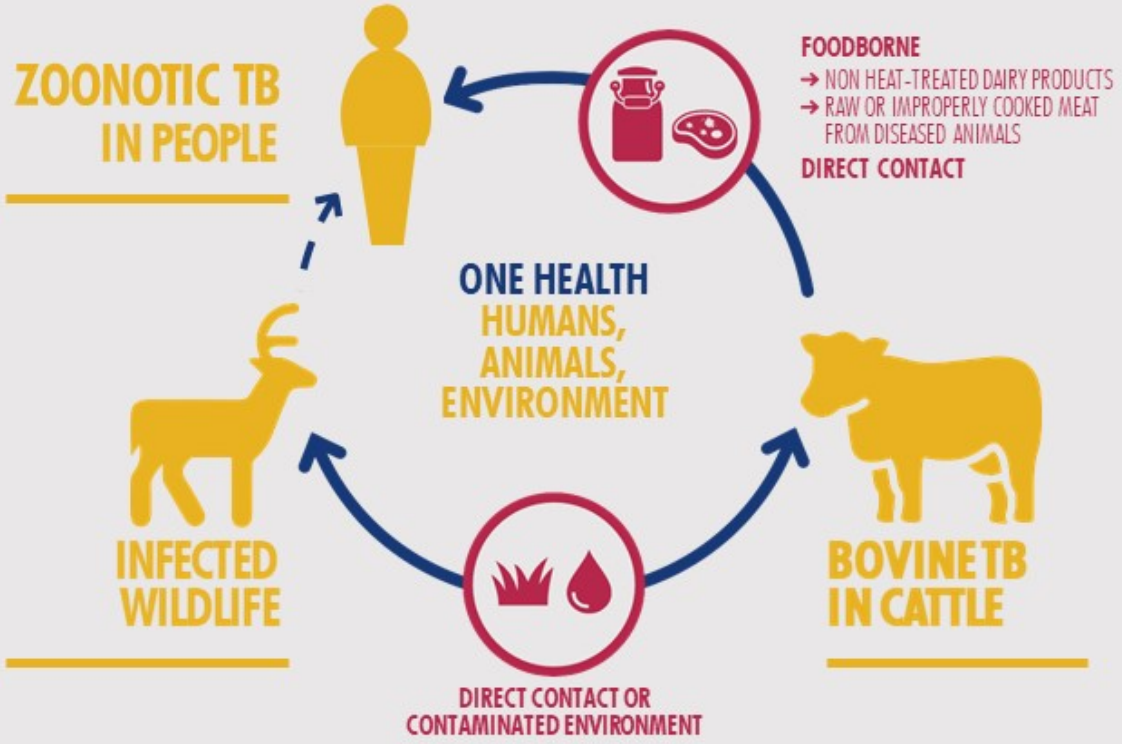
USDA U.S. Department of Agriculture

Mycobacterium Tuberculosis Complex (MTBC) species

- *Primary human pathogens*
  - *M. tuberculosis*
  - *M. africanum*
  - *M. canetti*
- *Primary animal pathogens*
  - *M. bovis*
  - *M. orygis*
  - *M. caprae*



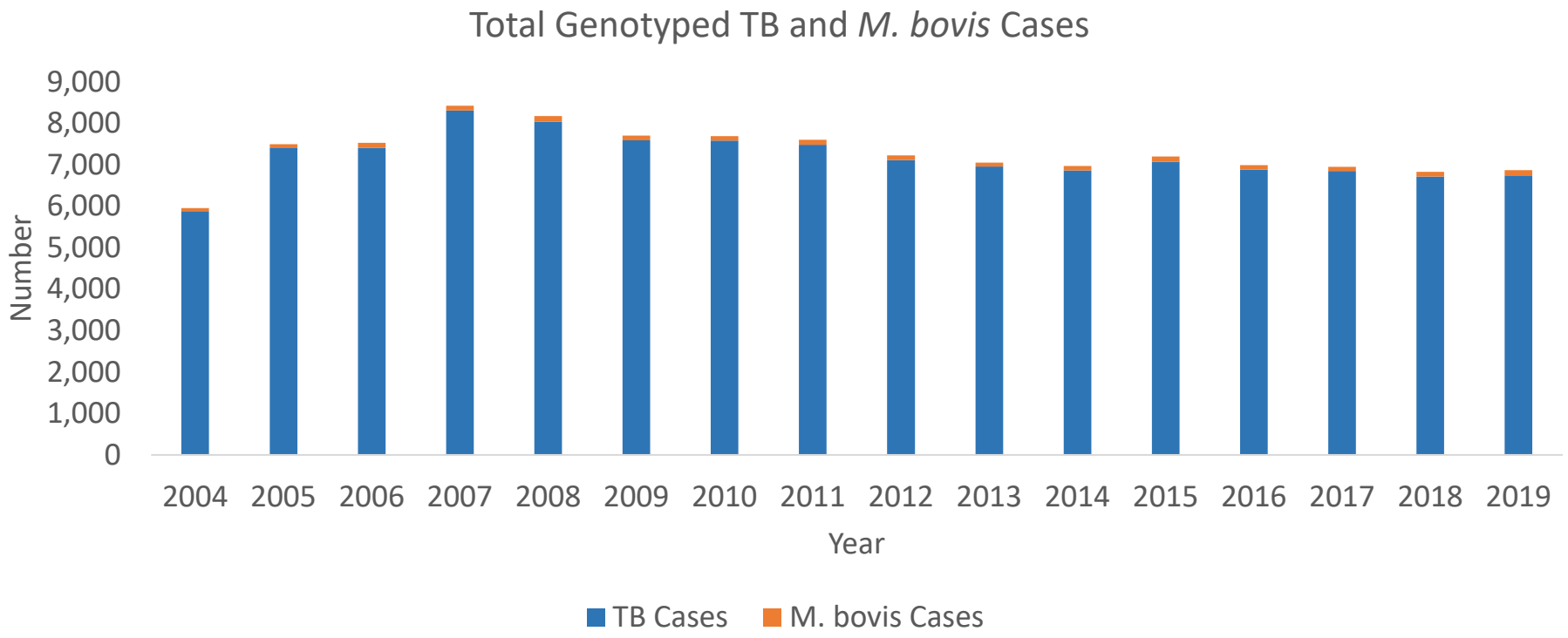
BREAKING THE CHAIN OF TRANSMISSION STOPPING ZOONOTIC AND BOVINE TUBERCULOSIS IN THEIR TRACKS



ACT NOW TO SAVE LIVES AND SECURE LIVELIHOODS

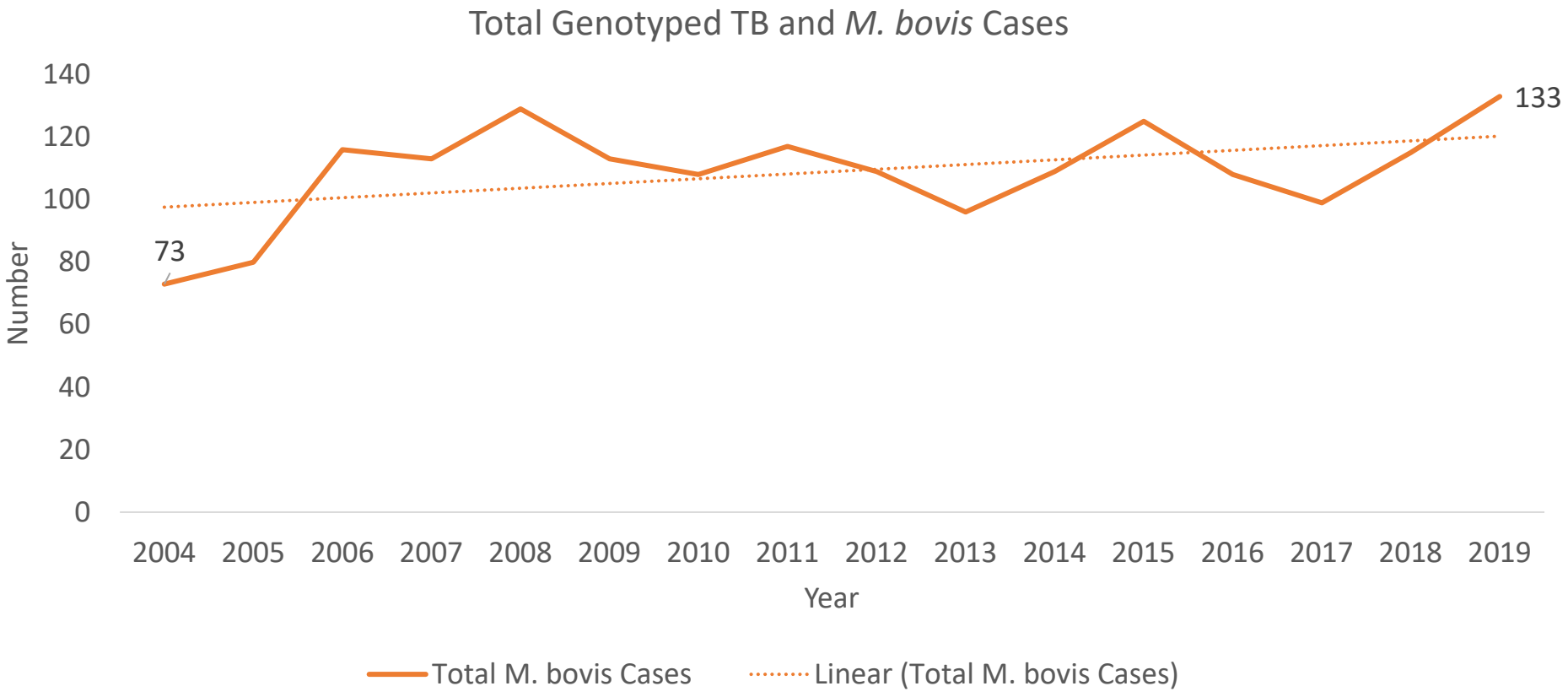
World Health Organization | OIE WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future* | Food and Agriculture Organization of the United Nations | The Union International Union Against Tuberculosis and Lung Disease

Human TB Burden



https://www.cdc.gov/tb/statistics/reports/2019/table18.htm

Human TB Burden



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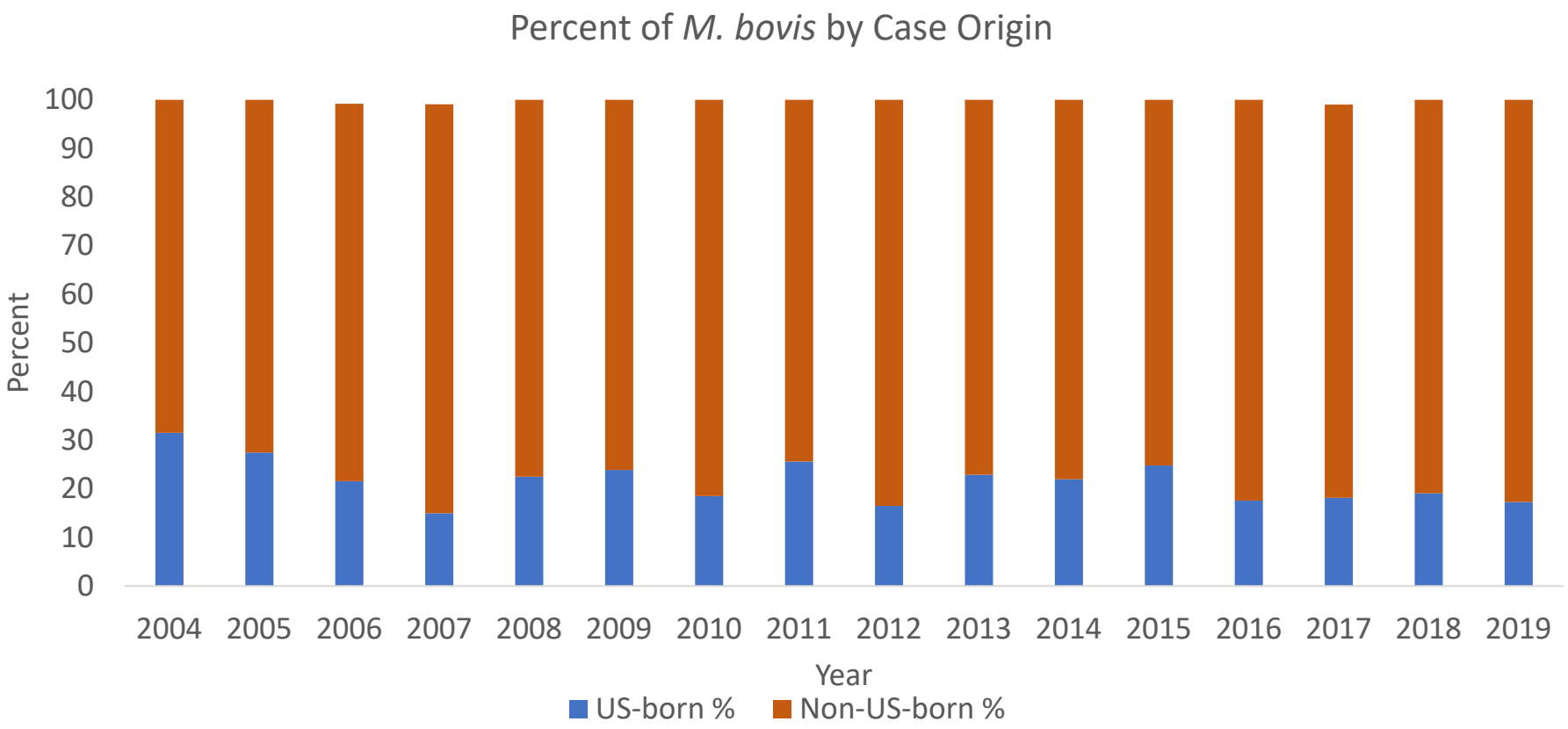
Human TB Burden



https://www.cdc.gov/tb/statistics/reports/2019/table18.htm

INT J TUBERC LUNG DIS 7(2):180–185

Epidemiology of *Mycobacterium bovis* disease in San Diego County, 1994–2000

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Human Tuberculosis due to *Mycobacterium bovis* in the United States, 1995–2005

Michele C. Hlavsa,[1,2] Patrick K. Moonan,[2] Lauren S. Cowan,[2] Thomas R. Navin,[2] J. Steve Kammerer,[2,3] Glenn P. Morlock,[2] Jack T. Crawford,[2] and Philip A. LoBue[2]

[1]Epidemic Intelligence Service, Office of Workforce and Career Development, and [2]Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, Sexually Transmitted Diseases, and Tuberculosis Prevention, Centers for Disease Control and Prevention, and [3]Northrup Grumman, Atlanta, Georgia

Clinical Infectious Diseases

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Human Tuberculosis Caused by *Mycobacterium bovis* in the United States, 2006–2013

Colleen Scott,[1,2] Joseph S. Cavanaugh,[2] Robert Pratt,[3] Benjamin J. Silk,[3] Philip LoBue,[3] and Patrick K. Moonan[2]

[1]Epidemic Intelligence Service, Division of Applied Sciences, [2]Division of Global HIV and TB, and [3]Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia

(See the Editorial Commentary by Fujiwara and Olea-Popelka on pages 602–3.)

Background. Using genotyping techniques that have differentiated *Mycobacterium bovis* from *Mycobacterium tuberculosis* since 2005, we review the epidemiology of human tuberculosis caused by *M. bovis* in the United States and validate previous findings nationally.

Methods. All tuberculosis cases with a genotyped *M. tuberculosis* complex isolate reported during 2006–2013 in the United States were eligible for analysis. We used binomial regression to identify characteristics independently associated with *M. bovis* disease using adjusted prevalence ratios (aPRs) and corresponding 95% confidence intervals (CIs).

Results. During 2006–2013, the annual percentages of tuberculosis cases attributable to *M. bovis* remained consistent nationally (range, 1.3%–1.6%) among all tuberculosis cases (N = 59 273). Compared with adults 25–44 years of age, infants aged 0–4 years (aPR, 1.9 [95% CI, 1.4–2.8]) and children aged 5–14 years (aPR, 4.0 [95% CI, 3.1–5.3]) had higher prevalences of *M. bovis* disease. Patients who were foreign-born (aPR, 1.4 [95% CI, 1.2–1.7]), Hispanic (aPR, 3.9 [95% CI, 3.0–5.0]), female (aPR, 1.4 [95% CI, 1.3–1.6]), and resided in US-Mexico border counties (aPR, 2.0 [95% CI, 1.7–2.4]) also had higher *M. bovis* prevalences. Exclusively extrapulmonary disease (aPR, 3.7 [95% CI, 3.3–4.2]) or disease that was both pulmonary and extrapulmonary (aPR, 2.4 [95% CI, 2.1–2.9]) were associated with a higher prevalence of *M. bovis* disease.

Conclusions. Children, foreign-born persons, Hispanics, and females are disproportionately affected by *M. bovis*, which was independently associated with extrapulmonary disease. Targeted prevention efforts aimed at Hispanic mothers and caregivers are warranted.

Keywords. *Mycobacterium bovis*; tuberculosis; epidemiology; trends.

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- Prevalence higher in
  - Foreign born, Hispanics, children (5-14 yrs.), and women
- Clinical Presentation

Lesion Location	*M. bovis*	*M. tuberculosis*
Extrapulmonary only	43.6%	15.6%
Pulmonary only	35.4%	74.3%
Both	21.0%	10.1%

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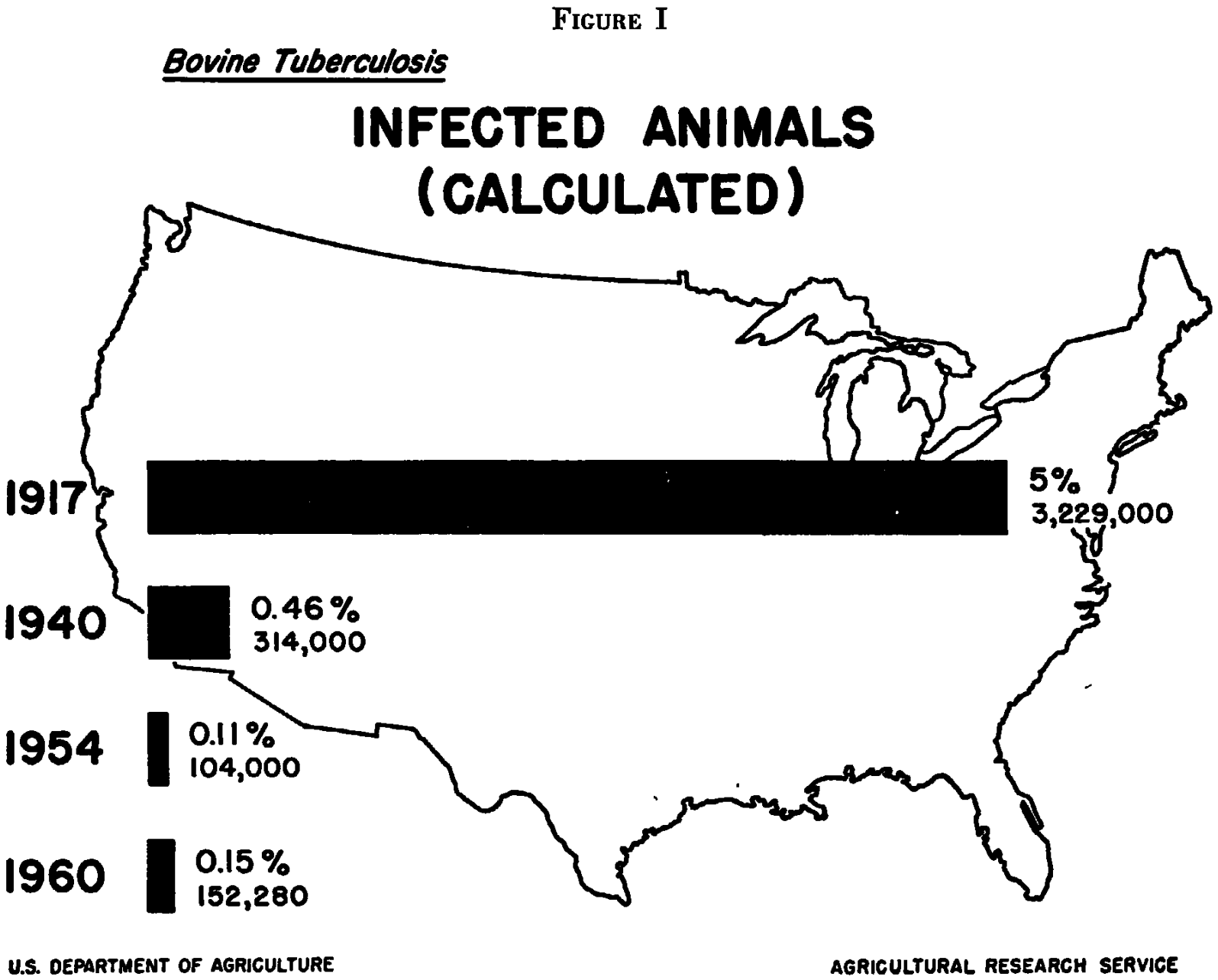
ARS slide of Reduction in TB Infected Animals.

(1960 USAHA TB Report)



Slide courtesy of Dr. Mark Camacho

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ARS slide of Reduction in TB Infected Animals.

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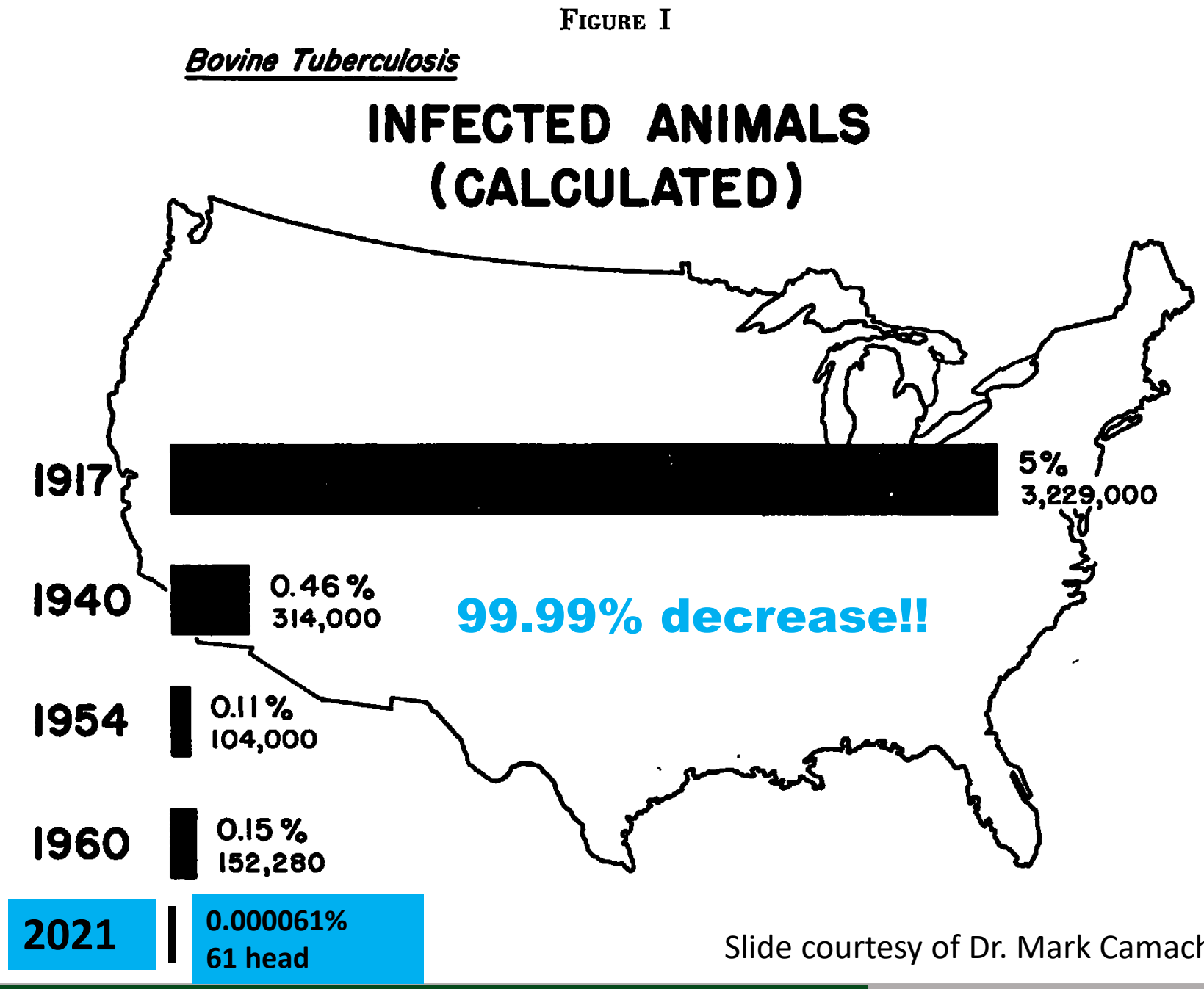

Slide courtesy of Dr. Mark Camacho

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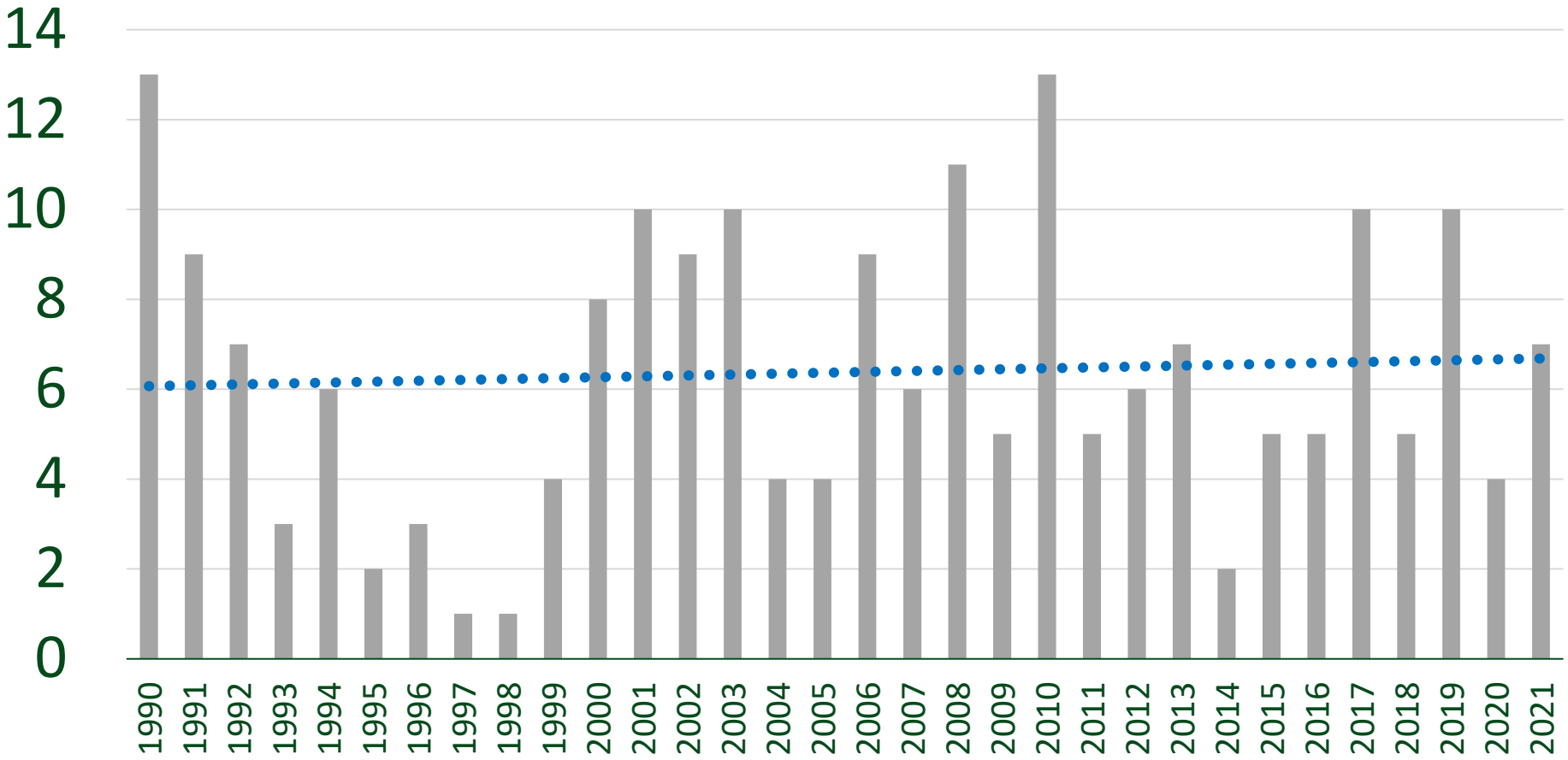
Cattle & Bison Affected Herds Over Time FY1990-2021 with linear trend line

The incidence of new cases of TB in the US is low, and relatively stable (upward trend), since 1990.



Slide courtesy of Dr. Mark Camacho

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Mystery of detecting NEW WGSs

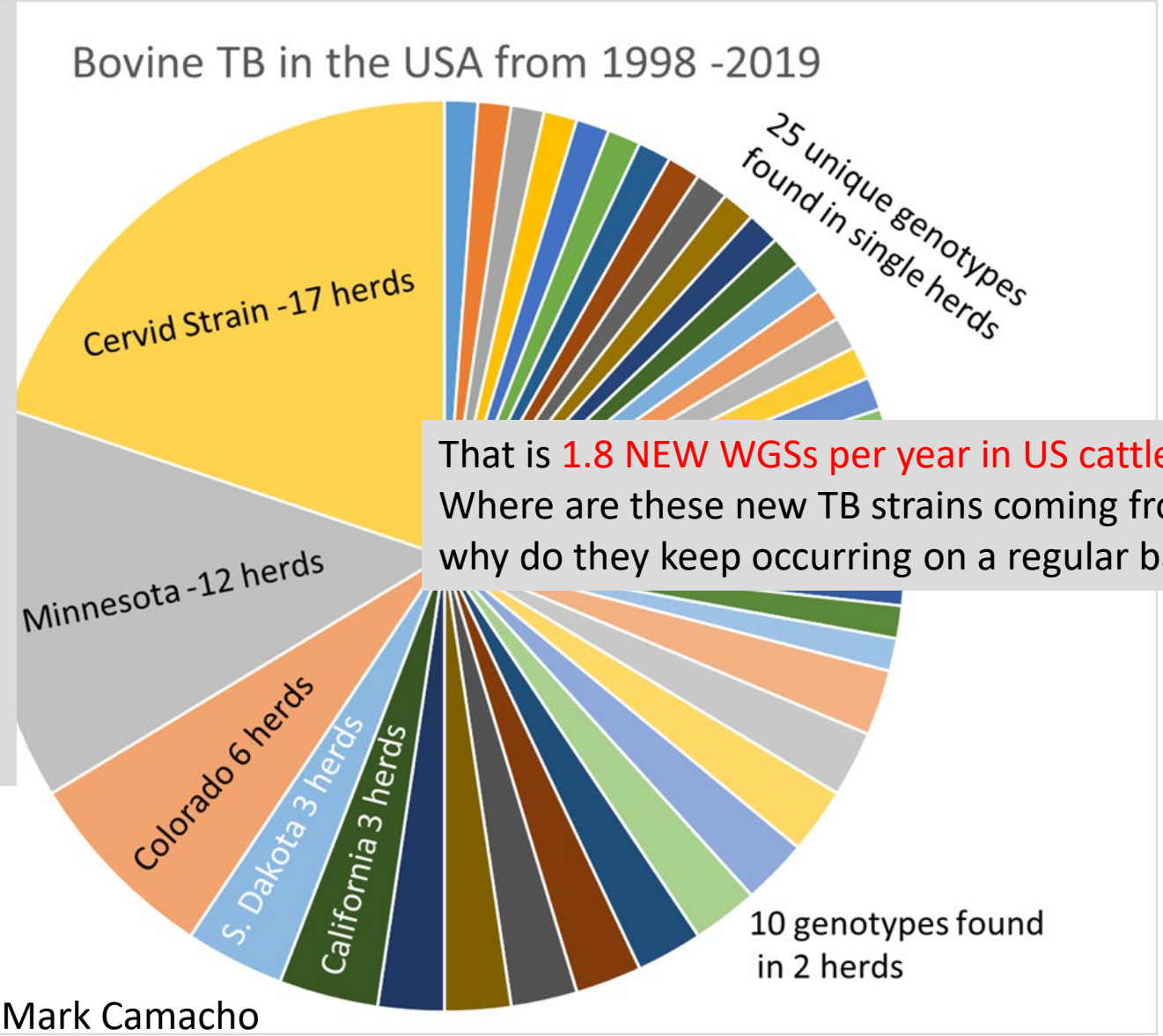
Each section of this pie-chart is a unique WGS of *M. bovis*.

Since 1998, the US has had 175 affected herds.

Without Michigan, the number is 91 affected herds with 42 unique, "never-before seen" TB strains in 23 years.

M. bovis Sources??

- Humans?
- Unknown cattle movements?
- Low level (percolating) infection in the US cattle herd?
- Import of infected Mexican cattle (feeders/ ropers)?



That is 1.8 NEW WGSs per year in US cattle! Where are these new TB strains coming from?... And why do they keep occurring on a regular basis?

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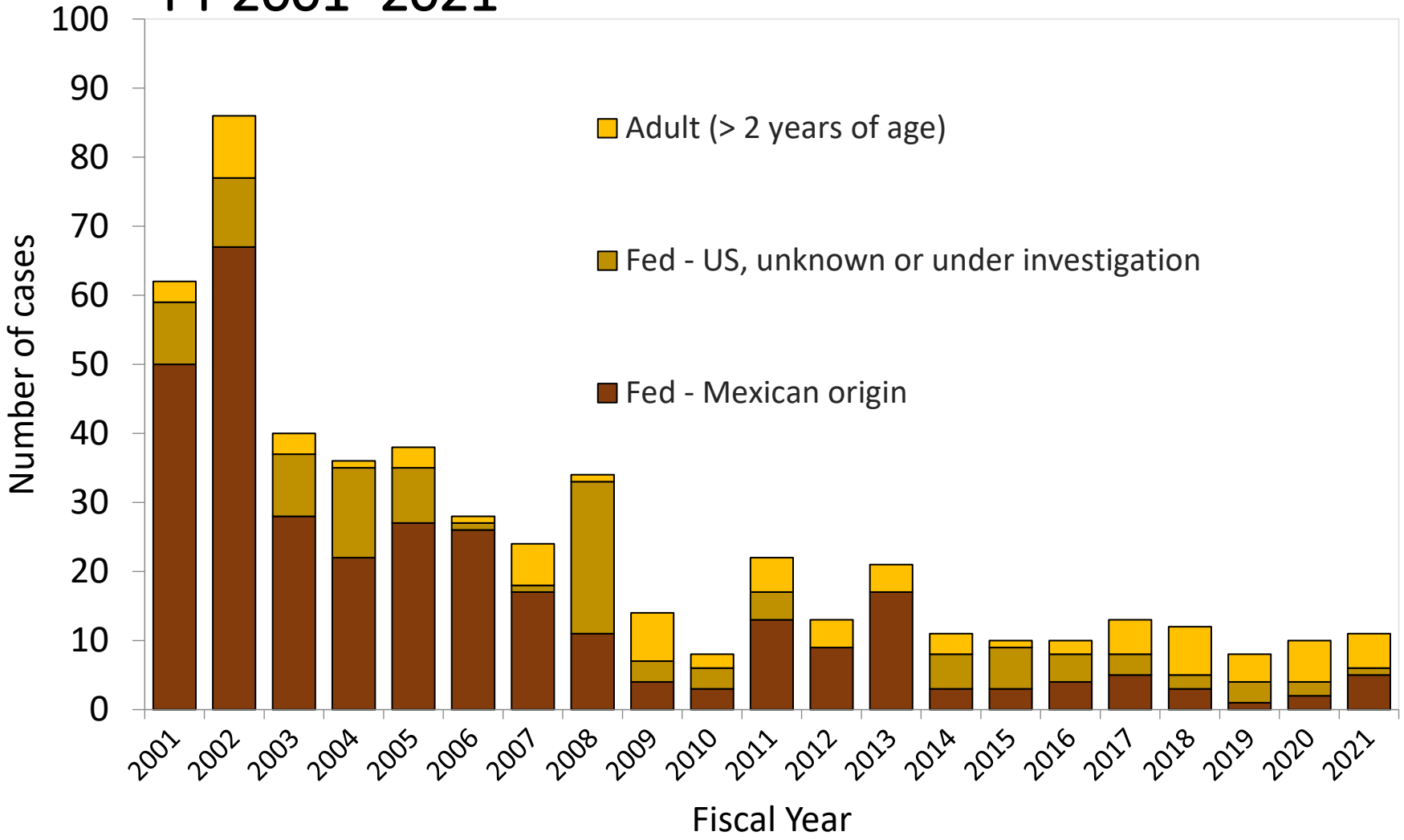
Slide courtesy of Dr. Mark Camacho

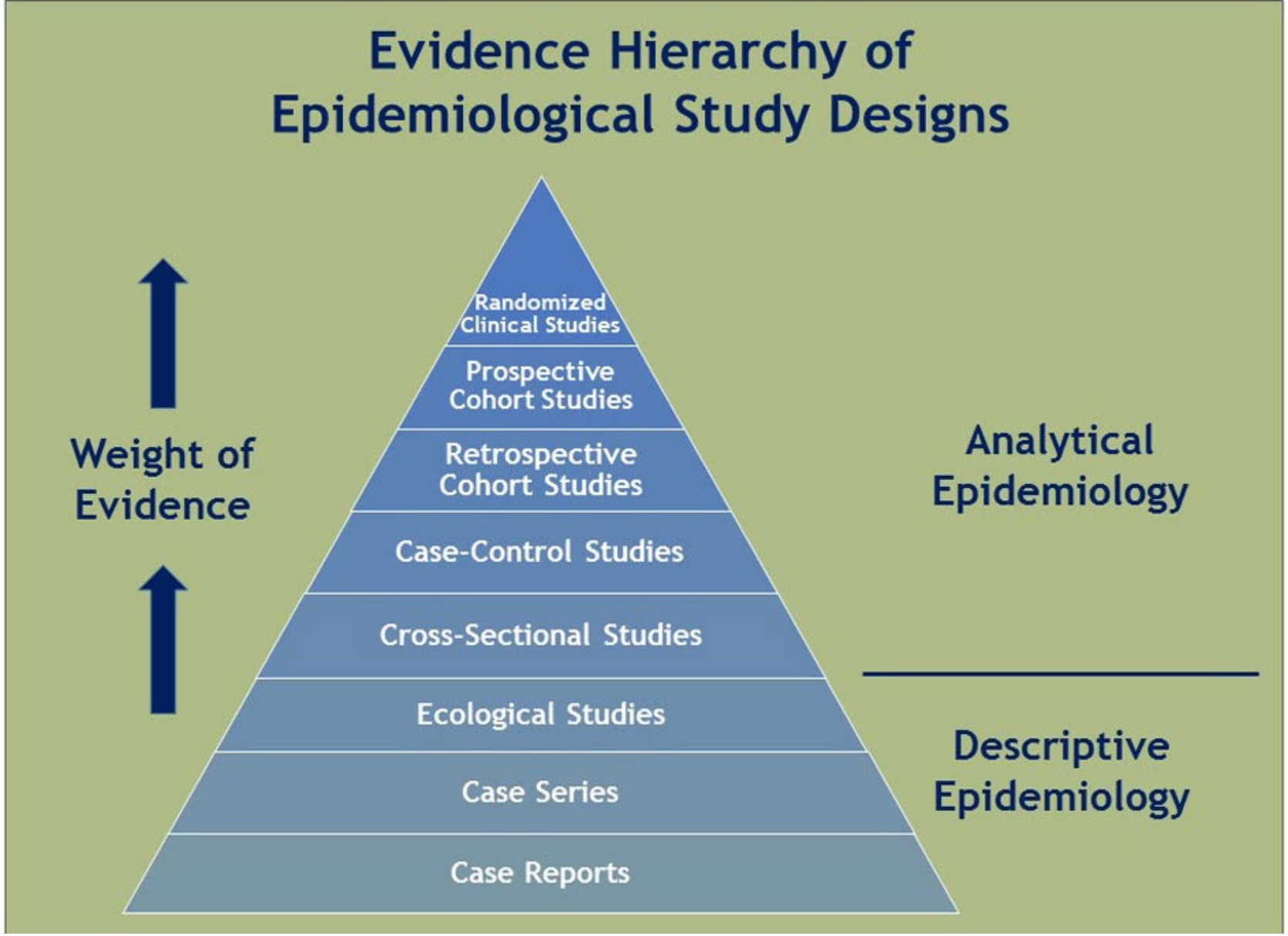
2021 Slaughter Surveillance

M. bovis Positive Cattle from Slaughter Surveillance, FY 2001–2021[1]



[1] 511 total cases including 82 in adult cattle; 429 cases in fed cattle including 320 cases (74%) in Mexican origin fed cattle

Slide courtesy of Dr. Mark Camacho



https://www.chemicalsafetyfacts.org/are-epidemiology-studies-good-tools-for-evaluating-chemical-safety/

Published U.S. cases

CASE REPORT 363

MAN A SOURCE OF BOVINE TUBERCULOSIS IN CATTLE

- 1942 – Tice, Cornell Vet (1944)
  - Owner contracted bovine TB (*M. bovis)* from original herd, developed pulmonary TB, subsequently infected 4 herds in 2.5 years

Published U.S. cases

PULMONARY BOVINE TUBERCULOSIS IN AN OWNER AND IN HIS DAIRY HERD

By JOHN H. BALDWIN*

New York State Department of Agriculture and Markets, Albany, New York

Received 11 Jan 1967

- 1966 – Baldwin, Cornell Vet (1968)
  - Owner contracted bovine TB from herd in 1947. Diagnosed with TB in 1965. Herd diagnosed in 1966.

Mycobacterium bovis in California dairies: A case series of 2002–2013 outbreaks

B. McCluskey[a,*], J. Lombard[b], S. Strunk[b], D. Nelson[c], S. Robbe-Austerman[d], A. Naugle[e], A. Edmondson[f]

Herd	Source of infection	Detection method
A	Unknown	Slaughter surveillance
B	Purchase of infected cattle from Herd A – probable	Trace from Herd A
C	Unknown	Slaughter surveillance
D[a]	Purchase of infected cattle from Herd E	Slaughter surveillance
E	Unknown	Trace from Herd D
F	Purchase of infected cattle from Herd E	Trace from Herd E
G	Unknown	Trace from Herd E
H	Unknown	Trace from Herd G
I	Unknown	Slaughter surveillance
J	Unknown	Slaughter surveillance
K	Contact with infected cattle from Herd J	Trace from Herd J
L	Contact with infected cattle from Herd A–probable	Slaughter surveillance

What has changed?

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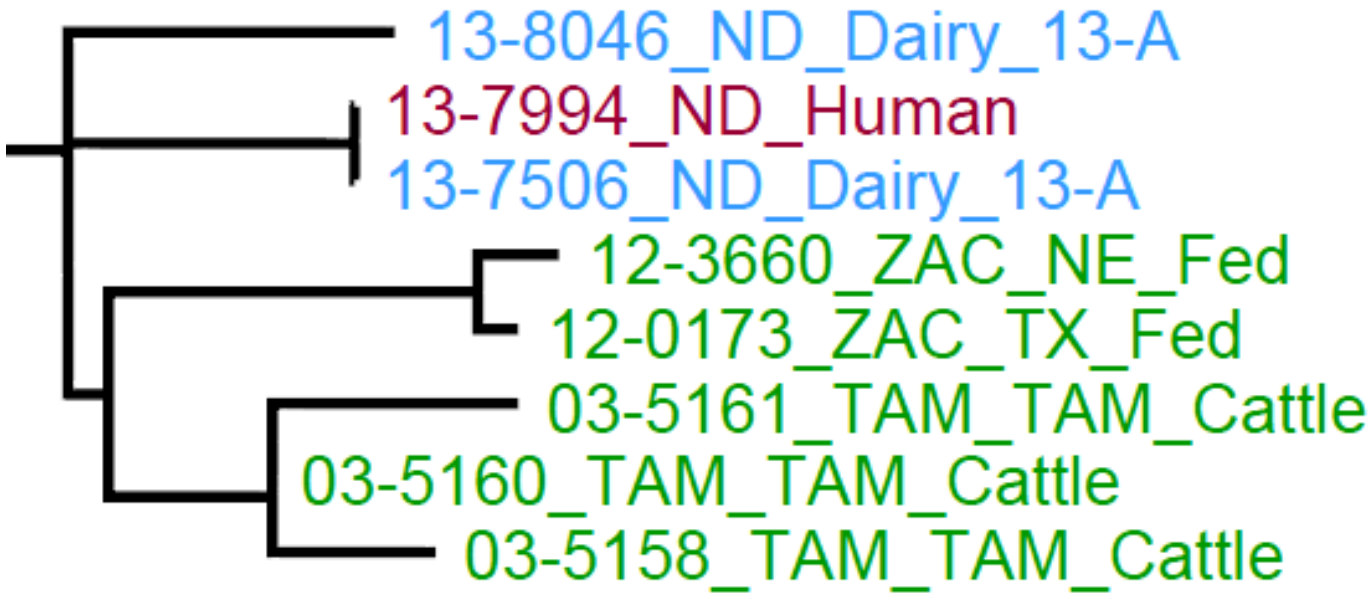
Recent U.S. cases

- North Dakota dairy herd
  - 2013
- Wisconsin dairy herd
  - 2015-2021
- Texas dairy heifer
  - 2018

North Dakota Dairy – 2013

- Dairy employee infected with *M. bovis* and alerted to State Ag by Public Health in October 2013
- Herd volunteered for testing in November 2013
  - ≥ 6 months of age tested
    - 319 tested; 11 Caudal fold tuberculin (CFT) test responders; 1 comparative cervical tuberculin (CCT) test suspect
      - 1 CCT suspect – necropsy –
        - Severe pneumonia w/ purulent abscesses
        - Mediastinal LN multiple micro abscesses
        - Culture POSITIVE
    - 10 CFT responder – slaughter
      - 1 cow was culture POSITIVE/PCR negative
      - 1 cow was culture negative/PCR POSITIVE

North Dakota Dairy – 2013



North Dakota Dairy – 2013

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13-7506_ND_Dairy_13-A	A	C	A	G	A	C	G	G	A	G	T	A	T	T	A	G	C	C	A	G	G	A	C	G	G	G	A	C	A	C	C	T	G	G	T	G	T	G	T	T	G	C	G
13-7994_ND_Human	A	C	A	G	A	C	G	G	A	G	T	A	T	T	A	G	C	C	A	G	G	A	C	G	G	G	A	C	A	C	C	T	G	G	T	G	T	G	T	T	G	C	G
13-8046_ND_Dairy_13-A	A	C	A	G	A	C	G	G	A	G	T	A	T	T	G	T	T	T	G	C	A	G	T	A	A	T	G	T	A	C	C	T	G	G	T	G	T	G	T	T	G	C	G

- WGS of employee and one cow matched
- ND investigation concluded:

"…employee was most likely infected and spread the disease to the cattle."

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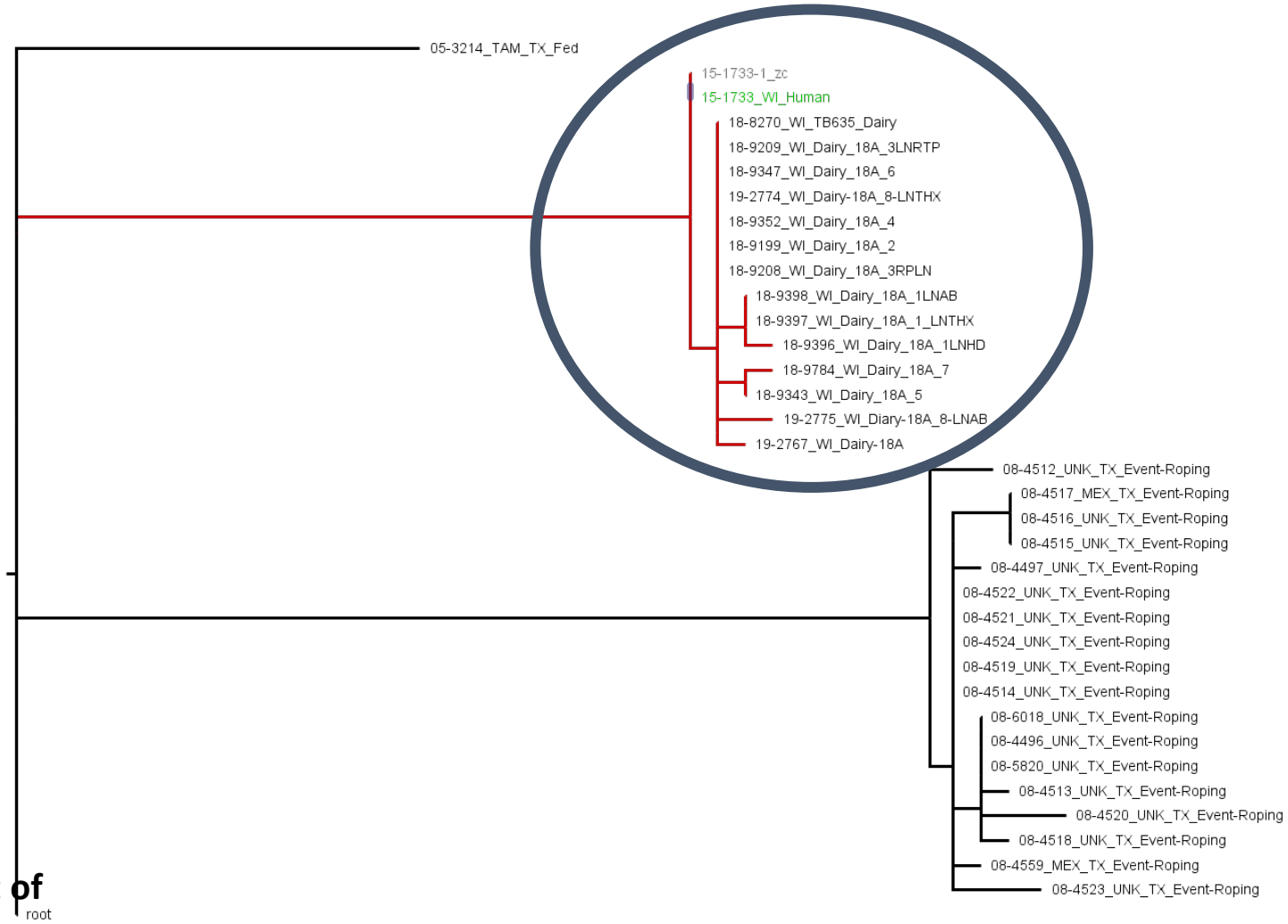
Wisconsin Dairy – 2015-20

- Infected dairy worker alerted to DATCP by DHS in April 2015, employed Jan – Mar 2015
- Herd volunteered for testing in May 2015
  - ~1500 tested; 31 CFT responders, 1 CCT suspect
    - CCT suspect – necropsy – NEGATIVE
  - Repeat testing in September 2015, 0 CCT suspects

Wisconsin Dairy – 2015-20

- Slaughter plant – 2018
  - Lesion – POSITIVE
  - Traced back to WI dairy, testing repeated
    - ~2000 tested (≥2 mo old): 48 CFT responders; 10 CCT S/R
    - 12 infected cows detected to date

Wisconsin Dairy – 2015-20



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Wisconsin Dairy – 2015-20

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- WGS of employee was very close to strains in cows

USDA **U.S. Department of Agriculture**

Texas dairy-cross heifer – 2018

- Transported from NM at 1 day of age, raised at a heifer raising facility in TX
- CFT responder and CCT reactor → necropsy
  - *Mycobacterium tuberculosis*

Doesn't normally occur in cattle, human exposure

Published U.S. cases

- North Dakota dairy herd
  - 2013
- Wisconsin dairy herd
  - 2015-2021
- Texas dairy heifer
  - 2018

frontiers in Veterinary Science

ORIGINAL RESEARCH
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Human-to-Cattle *Mycobacterium tuberculosis* Complex Transmission in the United States

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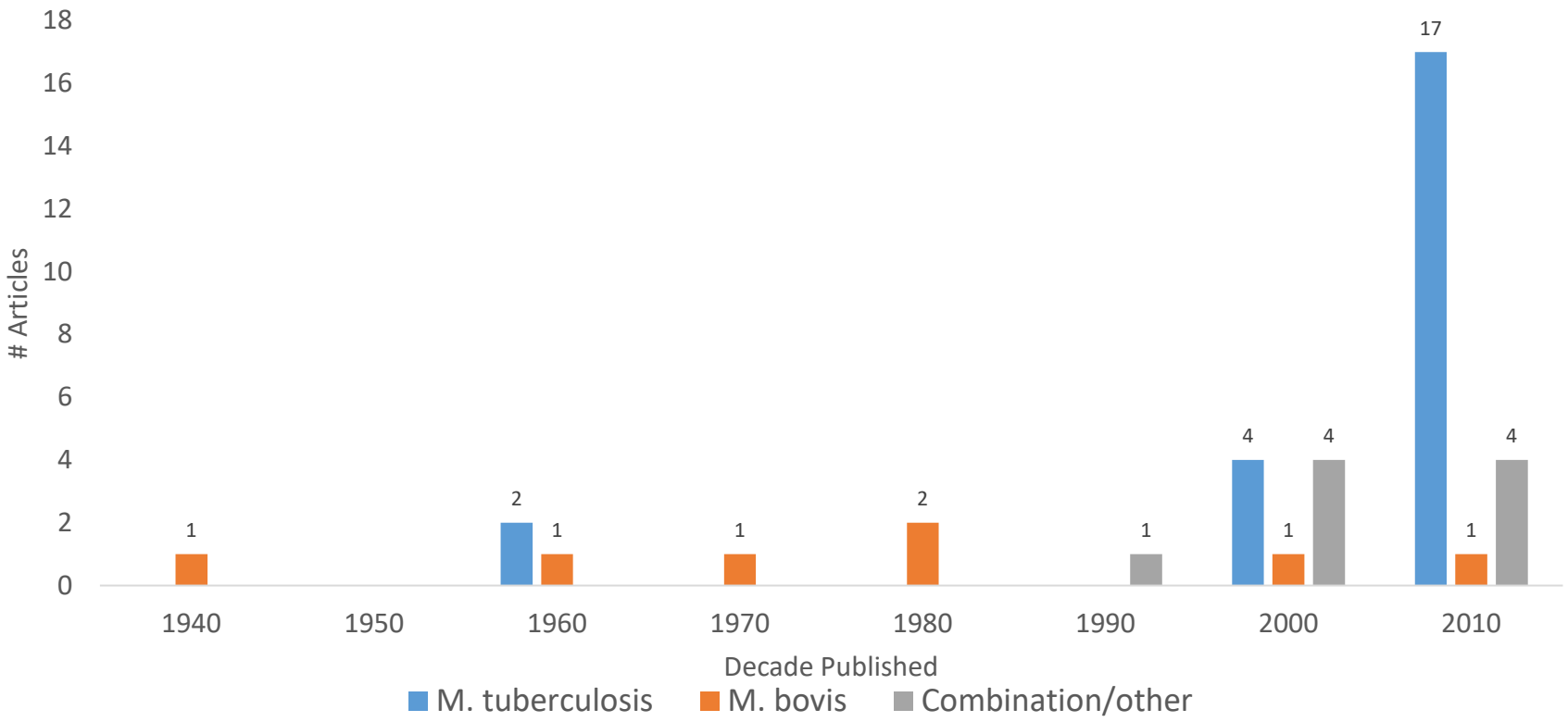
The *Mycobacterium tuberculosis* complex (MTBC) species includes both *M. tuberculosis*, the primary cause of human tuberculosis (TB), and *M. bovis*, the primary cause of bovine tuberculosis (bTB), as well as other closely related *Mycobacterium* species. Zoonotic transmission of *M. bovis* from cattle to humans was recognized more than a century ago, but transmission of MTBC species from humans to cattle is less often recognized. Within the last decade, multiple published reports from around the world describe human-to-cattle transmission of MTBC. Three probable cases of human-to-cattle MTBC transmission have occurred in the United States since 2013. In the first case, detection of active TB disease (*M. bovis*) in a dairy employee in North Dakota prompted testing and ultimate detection of bTB infection in the dairy herd. Whole genome sequencing (WGS) demonstrated a match between the bTB strain in the employee and an infected cow. North Dakota animal and public health officials concluded that the employee's infection was the most likely source of disease introduction in the dairy. The second case involved a Wisconsin dairy herd with an employee diagnosed with TB disease in 2015. Subsequently, the herd was tested twice with no disease detected. Three years later, a cow originating from this herd was detected with bTB at slaughter. The strain in the slaughter case matched that of the past employee based on WGS. The third case was a 4-month-old heifer calf born in New Mexico and transported to Texas. The calf was TB tested per Texas entry requirements and found to have *M. tuberculosis*. Humans are the suspected source of *M. tuberculosis* in cattle; however, public health authorities were not able to identify an infected human associated with the cattle operation. These three cases provide strong evidence of human-to-cattle transmission of MTBC organisms and highlight human infection as a

USDA U.S. Department of Agriculture

What about other countries?

Number of Published Studies by MTBC Species and Decade Published



USDA U.S. Department of Agriculture

INT J TUBERC LUNG DIS 8(7):903–904

SHORT COMMUNICATION

Mycobacterium bovis tuberculosis: from animal to man and back

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SUMMARY

Rare cases of tuberculosis due to *Mycobacterium bovis* have been described in humans who have been exposed to cattle or other infected animals. We report a case of tuberculosis in cattle exposed to a patient infected with *M. bovis*, where the strain isolated in the cattle and the patient were identical. As the patient is reported to have been exposed and contaminated during childhood, this seems to be the first documented case of transmission of *M. bovis* from animal to man and back to animal.

KEY WORDS: *M. bovis* tuberculosis; animal tuberculosis; contamination

JOURNAL OF CLINICAL MICROBIOLOGY, July 2005, p. 3555–3557 Vol. 43, No.
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Transmission of *Mycobacterium tuberculosis* from Human to Cattle

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Received 15 September 2004/Returned for modification 29 November 2004/Accepted 3 April 2005

We describe the first transmission of *Mycobacterium tuberculosis* from human to cattle confirmed by molecular typing of isolates involved in the transmission. IS*6110*-based restriction fragment length polymorphism analysis showed that the isolates from the cattle and farm worker who suffered from pulmonary tuberculosis 1 year prior to this case were the same strains.

JCM
Journals.ASM.org

CASE REPORT

Transmission of *Mycobacterium orygis* (*M. tuberculosis* Complex Species) from a Tuberculosis Patient to a Dairy Cow in New Zealand

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Animal Health Board, Wellington, New Zealand[a]; Waikato District Health Board, Hamilton, New Zealand[b]; and AgResearch, NCBID Wallaceville, Upper Hutt, New Zealand[c]

***Mycobacterium orygis*, previously called the oryx bacillus, is a member of the *Mycobacterium tuberculosis* complex and has been reported only recently as a cause of human tuberculosis in patients of South Asian origin. We present the first case documenting the transmission of this organism from a human to a cow.**

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Short Communication

Mycobacterium tuberculosis infection in grazing cattle in central Ethiopia

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ABSTRACT

A preliminary study to characterise mycobacteria infecting tuberculous cattle from two different management systems in central Ethiopia was carried out. Approximately 27% of isolates from grazing cattle were *Mycobacterium tuberculosis*, while cattle in a more intensive-production system were exclusively infected with *M. bovis*. The practice of local farmers discharging chewed tobacco directly into the mouths of pastured cattle was identified as a potential route of human-to-cattle transmission of *M. tuberculosis*.

Fig. 1. A farmer in central Ethiopia discharging tobacco juice directly into the oral cavity of his cattle, a common practice in this region and a possible route of transmission of *Mycobacterium tuberculosis* from humans to cattle.

"The practice of local farmers discharging chewed tobacco directly into the mouths of pastured cattle was identified as a potential route of human-to-cattle transmission of M. tuberculosis."

Epidem. Inf. (1987), **92**, 221–234
Printed in Great Britain

SPECIAL ARTICLE

Bovine tubercle bacilli and disease in animals and man

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Proven cases of transmission of bovine tubercle bacilli from man to cattle have been reported (Leslie, 1968; Lepper & Corner, 1983). Although transmission is often via the respiratory route, a number of cases of cross-infection resulted from attendants urinating on the hay. This, we are credibly informed, is a common practice and is said to provide a source of salt in the cows' diet! Huitema (1969) reported 50 examples of herds infected from human sources and in 24 cases the responsible individual had renal tuberculosis. Many of these patients, especially the older ones, had clear chest radiographs and only vague symptoms. Diagnosis was thus often delayed until many animals had been infected. As noted above, urinary tract infection is nowadays one of the more frequent manifestations of human tuberculosis due to bovine strains.

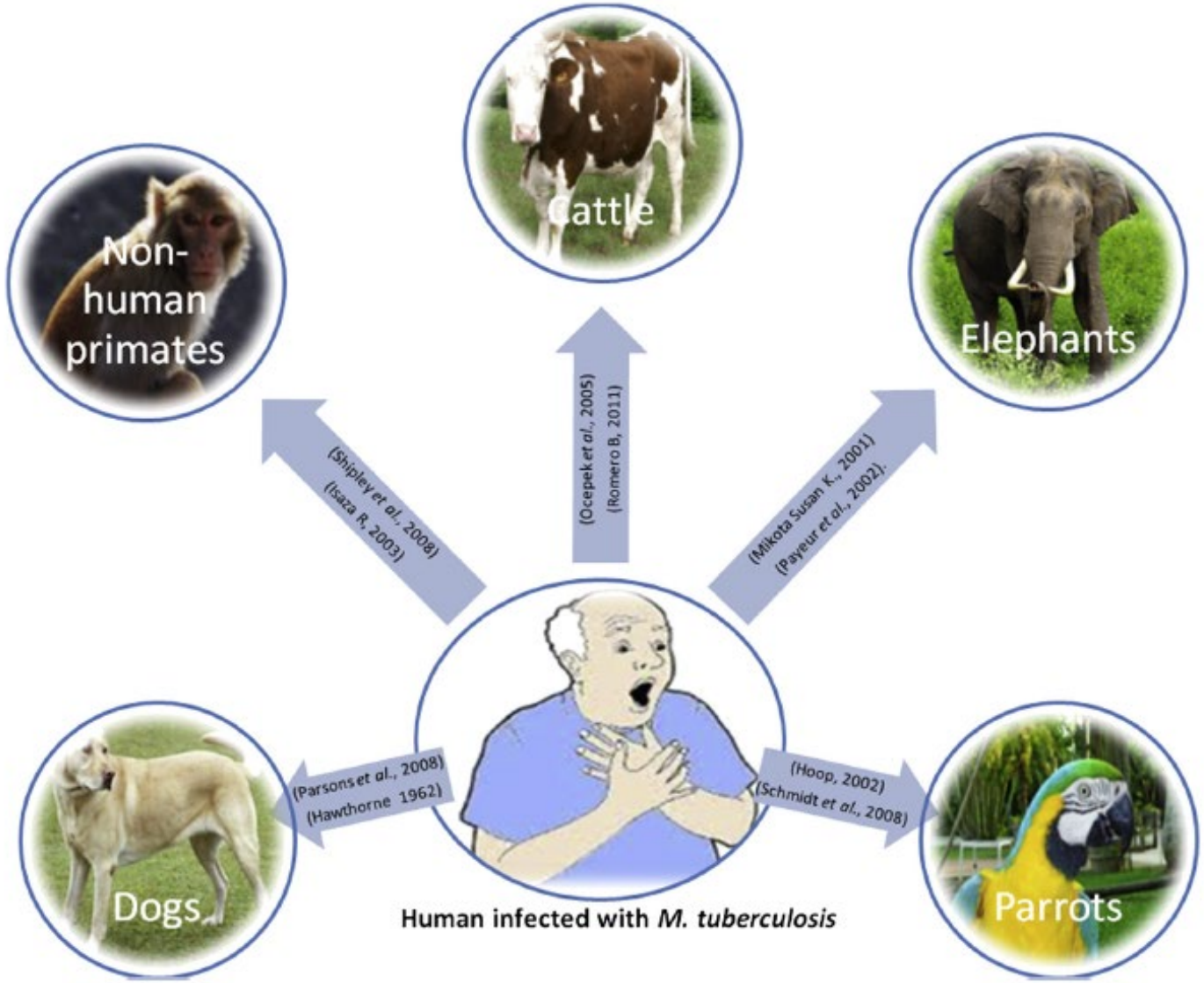
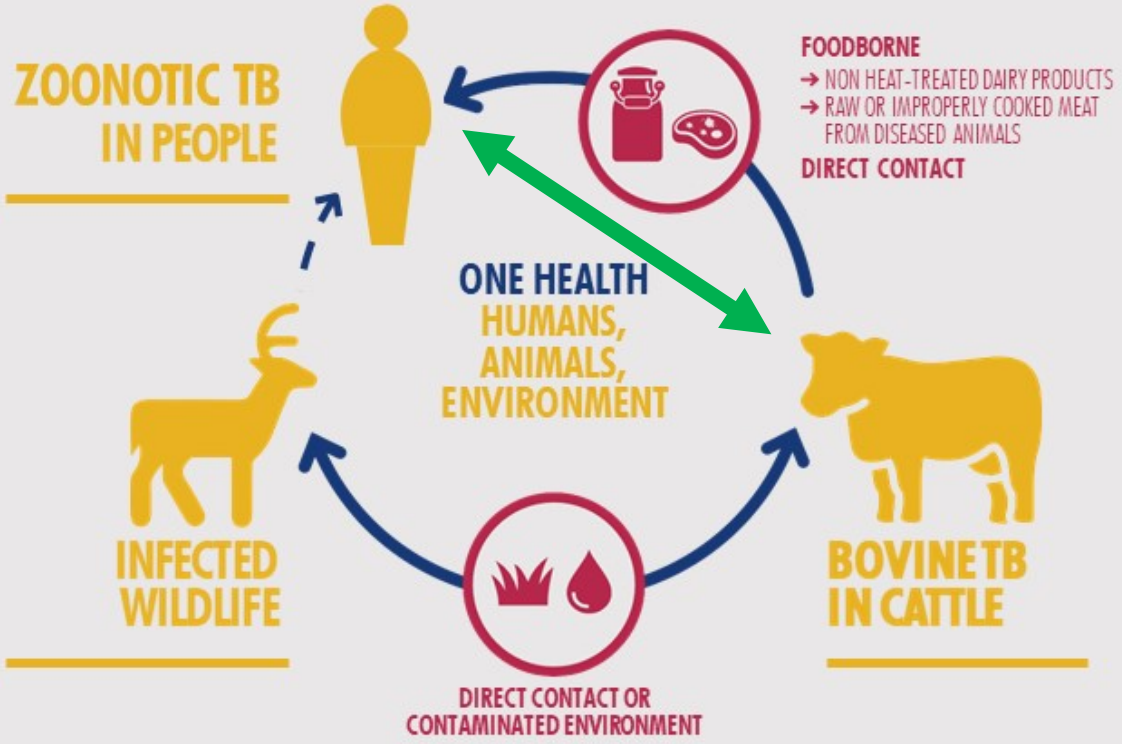


Figure 2. Anthroponotic tuberculosis in animals in contacts with *M. tuberculosis*-infected human hosts.

BREAKING THE CHAIN OF TRANSMISSION STOPPING ZOONOTIC AND BOVINE TUBERCULOSIS IN THEIR TRACKS



ACT NOW TO SAVE LIVES AND SECURE LIVELIHOODS

World Health Organization | OIE WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future* | Food and Agriculture Organization of the United Nations | The Union International Union Against Tuberculosis and Lung Disease

Conclusions

- U.S. cattle herds continue to become infected
- Source is unknown for more than 40%
- Three relatively recent U.S. cases show evidence of human-to-cattle transmission of MTBC species
- Multiple reports of human-to-cattle transmission of MTBC species from around the world
- One Health approach needed to address this issue

Activities

- National Milk Producers Federation TB Working Group
  - Led by Miquela Hanselman and Jamie Jonker
  - Animal and public health, industry, producers
  - Best practices for human-to-cattle TB transmission issues
    - Effectively communicate the risk to public health
    - Communication between animal and public health when TB is detected
    - Managing risk of human-to-cattle transmission on dairies
      - Testing of employees

NMPF
NATIONAL MILK PRODUCERS FEDERATION

Thank You!

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